

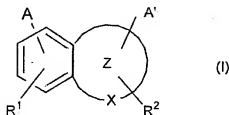
APPLICANT(S): ZIV, Ilan et al.  
SERIAL NO.: Not yet assigned  
FILED: Herewith  
Page 9

AMENDMENTS TO THE CLAIMS

Please cancel claims 1-41. Please add new claims 42-67 as follows.

Claims 1-41 (Cancelled)

42. (New) A method for selective targeting of a chemical compound to a cell undergoing perturbation of the normal organization of its plasma membrane (PNOM-cell) present in a cell population, comprising the steps of: (i) contacting the cell population with a PMBC, being a chemical compound represented by the structure set forth in formula (I):



wherein Z represents null, or a ring system formed of cycloalkyl, cycloalkenyl, heterocyclyl, aryl or heteroaryl groups or combinations of such groups, the ring system consisting of 5, 6, 7, 8, 9 or 10 atoms;

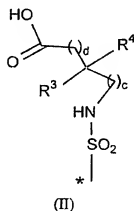
X represents an atom, which is C, N, O or S, where each of these atoms may bear 0, 1 or 2 hydrogen atoms according to the meaning of Z;

R<sup>1</sup> and R<sup>2</sup> are each independently hydrogen, halogen, hydroxyl, -NO<sub>2</sub> group or W-Q<sub>b</sub>; wherein W is null, nitrogen, oxygen or carbon; and Q represents hydrogen, a C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkyl, hydroxyalkyl, or straight or branched haloalkyl, wherein Q groups may be either the same or different; and b is an integer, being 1 when W is oxygen or null; 2 in the case that W is nitrogen; or 3 in the case that W is a carbon atom;

A and A' are each a radical independently selected from one of the following four groups:

- i) hydrogen;
- ii) SO<sub>3</sub>H, and L-SO<sub>3</sub>H, wherein L stands for a C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub> or C<sub>5</sub> alkylene linker;

iii) a structure, set forth in formula II:

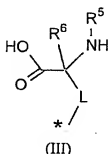


wherein  $R^3$  is hydrogen,  $(CH_2)_p-OH$ ,  $(CH_2)_p-SH$ ,  $(CH_2)_p-F$ , or suspected of comprising such PNOM cell, comprising the steps of contacting a cell population with a compound represented by a radical of  $C_1$ ,  $C_2$ ,  $C_3$ , or  $C_4$  carboxylic acid, wherein  $p$  is 1, 2, or 3;

$R^4$  is hydrogen, a  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$  straight or branched alkyl, a  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$  straight or branched hydroxyalkyl or a  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$  straight or branched fluoroalkyl;

$c$  and  $d$  are each an integer of 0 or 1;  $c$  and  $d$  may be the same or different; \* represents the point of attachment to the structure of formula (I); or

iv) a structure set forth in formula (III):



wherein  $R^5$  and  $R^6$  are independently hydrogen,  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$  straight or branched alkyl,  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$  straight or branched hydroxyalkyl or  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$  straight or branched haloalkyl;  $R^5$  and  $R^6$  can be the same or different; and  $L$  stands for null

APPLICANT(S): ZIV, Ilan et al.  
SERIAL NO.: Not yet assigned  
FILED: Herewith  
Page 11

or a C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub> or C<sub>5</sub> alkylene linker; \* represents the point of attachment to the structure of formula (I);

wherein when at least one of A or A' groups is other than hydrogen, and is different than the structure of formula (III);

thereby selectively targeting the chemical compound to the PNOM-cells within the cell population.

43. (New) A method of detecting the presence of PNOM-cells within a cell population, comprising the steps of:

(i) administering the cell population with a PMBC, or a conjugate comprising said PMBC and a marker for imaging, wherein said PMBC is represented by the structure set forth in formula (I) of Claim 42, wherein A, A', X, Z, R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup>, L, c and d are as defined in Claim 42; and

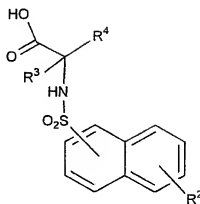
(ii) determining the amount of PMBC bound to cells in the cell population wherein a bound amount which is significantly higher than a control indicates the presence of PNOM-cells within the cell population.

44. (New) A method according to Claim 42, wherein the PNOM- cell is a cell undergoing a death process, an apoptotic cell or an activated platelet.

45. (New) A method according to Claim 42, wherein in the compound represented by the structure as set forth in formula (I) A or A' are represented by formula (II), R<sup>1</sup> is hydrogen, and R<sup>2</sup> is NQ<sub>2</sub>, wherein Q groups may be the same or different, each being a hydrogen or a C<sub>1</sub>-C<sub>4</sub> alkyl.

46. (New) A method according to Claim 42, wherein said PMBC is represented by the structure as set forth in formula (IV):

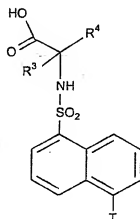
APPLICANT(S): ZIV, Ilan et al.  
 SERIAL NO.: Not yet assigned  
 FILED: Herewith  
 Page 12



(IV)

wherein  $R^2$ ,  $R^3$  and  $R^4$  are as defined in Claim 42.

47. (New) A compound represented by a structure as set forth in formula (V):

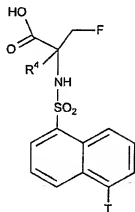


(V)

wherein T is  $-OH$ ,  $-O-CH_3$ ,  $-O-(CH_2)_yCH_3$ ,  $NH_2$ ,  $N(CH_3)_2$ ,  
 $N[(CH_2)_3CH_3]_2$ ,  $-N(CH_3)[(CH_2)_2CH_3]$ ,  $-N(CH_3)CH_2CH_3$  or  $-N(CH_3)[(CH_2)_3CH_3]$ ; y stands  
 for an integer of 1, 2, or 3; and  $R^3$  and  $R^4$  are each as defined in Claim 42.

APPLICANT(S): ZIV, Ilan et al.  
SERIAL NO.: Not yet assigned  
FILED: Herewith  
Page 13

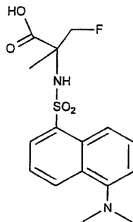
48.(New) A compound according to Claim 47, represented by the structure as set forth in formula (VI):



(VI)

wherein T is as defined in Claim 47, and R<sup>4</sup> is hydrogen or a C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> straight or branched alkyl, and wherein the F atom is <sup>18</sup>F or <sup>19</sup>F or mixtures of fluorine isotopes.

49. (New) A compound according to Claim 47, represented by the structure as set forth in formula (VII):

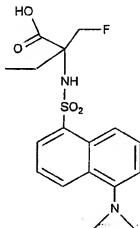


(VII)

APPLICANT(S): ZIV, Ilan et al.  
SERIAL NO.: Not yet assigned  
FILED: Herewith  
Page 14

wherein the F atom is  $^{18}\text{F}$  or  $^{19}\text{F}$  or mixture of fluorine isotopes.

50. (New) A compound according to Claim 47, represented by the structure as set forth in formula (VIII):

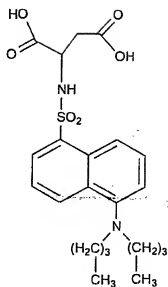


(VIII)

wherein the F atom is  $^{18}\text{F}$  or  $^{19}\text{F}$  or mixtures of fluorine isotopes.

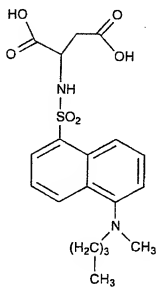
51. (New) A compound according to Claim 47 represented by the structure as set forth in formula (IX):

APPLICANT(S): ZIV, Ilan et al.  
 SERIAL NO.: Not yet assigned  
 FILED: Herewith  
 Page 15



(IX)

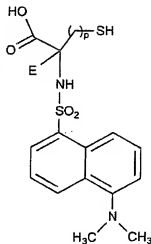
52. (New) A compound according to Claim 47, represented by the structure as set forth in formula (X):



(X)

APPLICANT(S): ZIV, Ilan et al.  
 SERIAL NO.: Not yet assigned  
 FILED: Herewith  
 Page 16

53.(New) A compound according to Claim 47, represented by the structure as set forth in formula (XI):

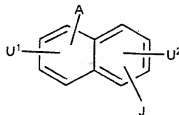


(XI)

wherein E is C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub> or C<sub>4</sub> alkyl; C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub> or C<sub>4</sub> fluoroalkyl; or C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub> or C<sub>4</sub> hydroxyalkyl; p stands for an integer of 1 or 2.

54. (New) A compound according to Claim 53, wherein p is 1.

55. (New) A method according to claim 42 comprising the step of contacting a cell population with a compound represented by the structure as set forth in formula (XII):



(XII)



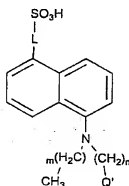
APPLICANT(S): ZIV, Ilan et al.  
 SERIAL NO.: Not yet assigned  
 FILED: Herewith  
 Page 17

wherein A is  $\text{SO}_3\text{H}$  or  $\text{L-SO}_3\text{H}$ , wherein L stands for a substituted or unsubstituted  $\text{C}_1$ ,  $\text{C}_2$ ,  $\text{C}_3$ ,  $\text{C}_4$  or  $\text{C}_5$  alkylene;

J is selected from  $\text{SO}_3\text{H}$ ,  $\text{L-SO}_3\text{H}$ , wherein L is as defined above, hydrogen and  $\text{W-Q}_b$ ; wherein W is null, nitrogen, oxygen or carbon; and Q represents hydrogen, a  $\text{C}_1$ ,  $\text{C}_2$ ,  $\text{C}_3$ ,  $\text{C}_4$ ,  $\text{C}_5$  or  $\text{C}_6$  straight or branched alkyl, straight or branched hydroxyalkyl, or straight or branched haloalkyl; wherein Q groups may be either the same or different; b is an integer, being 1 when W is oxygen or null, 2 in the case that W is nitrogen, or 3 in the case that W is a carbon atom;

$\text{U}^1$  and  $\text{U}^2$  are each halogen, halogen, hydroxyl,  $-\text{NO}_2$ ;  $\text{C}_1$ ,  $\text{C}_2$ ,  $\text{C}_3$ ,  $\text{C}_4$ ,  $\text{C}_5$  or  $\text{C}_6$  straight or branched alkyl;  $\text{C}_1$ ,  $\text{C}_2$ ,  $\text{C}_3$ ,  $\text{C}_4$ ,  $\text{C}_5$  or  $\text{C}_6$  straight or branched halo-alkyl;  $\text{C}_1$ ,  $\text{C}_2$ ,  $\text{C}_3$ ,  $\text{C}_4$ ,  $\text{C}_5$  or  $\text{C}_6$  straight or branched hydroxy-alkyl;  $\text{U}^1$  and  $\text{U}^2$  groups may be the same or different

56. (New) A method according to claim 55, comprising the step of contacting a cell population with a compound represented by the structure as set forth in formula (XIII):

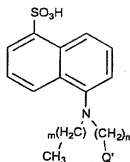


(XIII)

wherein n stands for an integer of 1, 2, 3, 4, 5 or 6, m stands for an integer of 0, 1, 2 or 3,  $\text{Q}'$  is hydrogen,  $-\text{OH}$  or  $-\text{F}$ , and L stands for null or  $\text{C}_1$ ,  $\text{C}_2$ ,  $\text{C}_3$ ,  $\text{C}_4$  or  $\text{C}_5$  alkylene, thereby selectively targeting a PNOM-cell in said cell population.

57. (New) A method according to claim 55, wherein said cell population is suspected of comprising such a PNOM-cell, comprising the step of contacting a cell population with a compound represented by the structure as set forth in formula (XIV);

APPLICANT(S): ZIV, Ilan et al.  
 SERIAL NO.: Not yet assigned  
 FILED: Herewith  
 Page 18



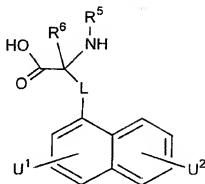
(XIV)

wherein  $n$  stands for an integer of 1, 2, 3, 4, 5 or 6,  $m$  stands for an integer of 0, 1, 2 or 3 and  $\text{Q}'$  is hydrogen,  $-\text{OH}$  or  $-\text{F}$ .

58. (New) A compound represented by the structure set forth in formula (XIV) wherein  $\text{Q}'$  is  $\text{F}$ , either  $^{18}\text{F}$  or  $^{19}\text{F}$  or a mixture of isotopes or wherein  $m$  is 0,  $n$  is 4 and  $\text{Q}'$  is hydrogen or wherein  $m$  is 0,  $n$  is 3 and  $\text{Q}'$  is hydroxyl or wherein  $m$  is 0,  $n$  is 4 and  $\text{Q}'$  is fluorine.

59. (New) A method according to claim 57, comprising the step of contacting a cell population with a compound represented by the structure as set forth in formula (XV):

APPLICANT(S): ZIV, Ilan et al.  
 SERIAL NO.: Not yet assigned  
 FILED: Herewith  
 Page 19



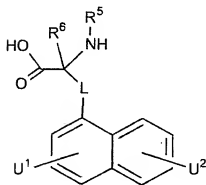
(XV)

wherein  $R^5$  and  $R^6$  are each independently hydrogen,  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$  straight or branched alkyl, straight or branched hydroxyalkyl or straight or branched fluoroalkyl;  $R^5$  and  $R^6$  can be the same or different;

$L$  stands for null or a  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$  or  $C_5$  alkylene linker;

$U^1$  and  $U^2$  are each hydrogen, halogen, hydroxyl,  $-NO_2$ ;  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  straight or branched alkyl;  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  straight or branched haloalkyl;  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  straight or branched hydroxyalkyl;  $U$  groups may be the same or different.

60. (New) A compound represented by the structure as set forth in formula (XV),

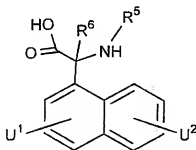


(XV)

APPLICANT(S): ZIV, Ilan et al.  
SERIAL NO.: Not yet assigned  
FILED: Herewith  
Page 20

wherein either  $U^1$  or  $U^2$  is fluorine or  $C_1$ ,  $C_2$ ,  $C_3$  or  $C_4$  fluoroalkyl, the F atom being either  $^{18}F$  or  $^{19}F$ .

61. (New) A compound represented by the structure as set forth in formula (XVI):



(XVI)

wherein  $R^5$  and  $R^6$  are independently hydrogen,  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$  straight or branched alkyl, straight or branched hydroxyalkyl or straight or branched fluoroalkyl;  $R^5$  and  $R^6$  can be the same or different;  $U^1$  and  $U^2$  are each hydrogen, halogen, hydroxyl,  $-NO_2$ ;  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  straight or branched alkyl;  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  straight or branched haloalkyl;  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$  or  $C_6$  straight or branched hydroxyalkyl; U groups may be the same or different.

62. (New) A compound according to claim 61 represented by the structure as set forth in formula (XVI), wherein  $R^5$  is  $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$  straight or branched alkyl, straight or branched hydroxyalkyl and straight or branched fluoroalkyl;  $R^6$  is  $C_2$ ,  $C_3$ ,  $C_4$ ,  $C_5$ ,  $C_6$  straight or branched alkyl, straight or branched hydroxyalkyl or straight or branched fluoroalkyl; and either  $U^1$  or  $U^2$  is other than hydrogen.

APPLICANT(S): ZIV, Ilan et al.  
SERIAL NO.: Not yet assigned  
FILED: Herewith  
Page 21

63. (New) A method of selective targeting PNOM-cells comprising the step of contacting a cell population with a compound represented by the structure as set forth claim 61.

64. (New) A method according to claim 43, comprising the steps of:

(i) contacting the cell population with a PMBC, or a conjugate comprising said PMBC and a marker for imaging, wherein said PMBC is represented by the structure set forth represented in any one of formulae I, IV, V, VI, VII, VIII, IX, X, XI, XII, XIII, XIV, XV or XVI; and

(II) determining the amount of PMBC bound to cells in said cell population, wherein a bound amount which is significantly higher than a control indicates the presence of PNOM-cells within the cell population.

65. (New) A compound according to Claim 47 wherein said compound is being linked either directly or through a linker Y to a member selected from a solid support, a marker for imaging or a therapeutic drug, wherein said linker Y is C<sub>1</sub>, C<sub>2</sub>, C<sub>3</sub>, C<sub>4</sub>, C<sub>5</sub> or C<sub>6</sub> alkylene, 5-6 atom aromatic or 5-6 heteroaromatic ring, wherein the heteroatom of said heteroaromatic ring is N, O and S, a metal chelator, or combinations thereof.

66. (New) An agent for the detection of PNOM-cells, comprising a compound according to claim 47, wherein said compound is linked or comprises a marker for imaging.

67. (New) An agent according to claim 66 wherein said marker for imaging is detectable by detector of color, fluorescence, X-ray, CT scan, MRI, radio-isotope scan, SPECT, or PET scan.